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This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1 - 60 (Cancelled)

Claim 61 (Currently Amended) A method of inhibiting the cleavage of TNF- α from cell membranes in a human comprising administering to such human an effective amount of a hydroxamic acid compound, or a pharmaceutically acceptable salt thereof, selected from the group consisting of:

(2R, 3S)-1-(4-benzyloxy-benzenesulfonyl)-3-methyl-piperazine-2-carboxylic acid

hydroxamide;

(2R, 3S)-3-methyl-1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-piperazine-2-

carboxylic acid hydroxamide;

(2R, 3S)-4-acetyl-3-methyl-1-[4-(2-methyl-benzyloxy)-benzenesulfonyl]-

piperazine-2-carboxylic acid hydroxamide;

(2S,3R,6S)-4-[4-(2,5-dimethyl-benzyloxy)-benzenesulfonyl]-2,6-dimethyl-

morpholine-3-carboxylic acid hydroxamide;

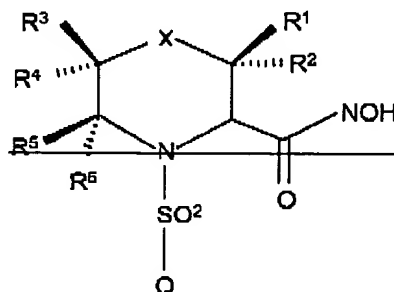
(2S,3R,6R)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-6-hydroxymethyl-2-

methyl-morpholine-3-carboxylic acid hydroxamide; and

(2S,3R,6R)-4-[4-(4-fluoro-benzyloxy)-benzenesulfonyl]-6-hydroxymethyl-2-

methyl-morpholine-3-carboxylic acid hydroxamide;

comprising the formula:



— or the pharmaceutically acceptable salt thereof, wherein

— X is oxygen, sulfur, SO, SO₂ or NR⁷;

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- ~~— R^1, R^2, R^3, R^4, R^5 and R^6 are selected from the group consisting of hydrogen, hydroxy, NH_2 , CN , $(C_1-C_6)alkyl$, $(C_2-C_6)alkenyl$, $(C_6-C_{10})aryl$, $(C_2-C_6)alkenyl$, $(C_2-C_9)heteroaryl$, $(C_2-C_6)alkenyl$, $(C_2-C_6)alkynyl$, $(C_6-C_{10})aryl$, $(C_2-C_6)alkynyl$, $(C_2-C_9)heteroaryl$, $(C_2-C_6)alkynyl$, $(C_1-C_6)alkylamino$, $[(C_1-C_6)alkyl]_2amino$, $(C_1-C_6)alkylthio$, $(C_1-C_6)alkoxy$, $perfluoro(C_1-C_6)alkyl$, $perfluoro(C_1-C_6)alkoxy$, $(C_6-C_{10})aryl$, $(C_2-C_9)heteroaryl$, $(C_6-C_{10})arylamino$, $(C_6-C_{10})arylthio$, $(C_6-C_{10})aryloxy$, $(C_2-C_9)heteroarylamino$, $(C_2-C_9)heteroarylthio$, $(C_2-C_9)heteroaryloxy$, $(C_2-C_6)cycloalkyl$, $(C_1-C_6)alkyl(hydroxymethylene)$, $piperidyl$, $(C_1-C_6)alkylpiperidyl$, $(C_1-C_6)acyl$, $(C_1-C_6)acylamino$, $(C_1-C_6)acylthio$, $(C_1-C_6)acyloxy$, $(C_1-C_6)alkoxy(C=O)$, CO_2H , $H_2N(C=O)$, $(C_1-C_6)alkylNH(C=O)$, and $[(C_1-C_6)alkyl]_2N(C=O)$;~~
- ~~— wherein said $(C_1-C_6)alkyl$ is optionally substituted by one or two groups selected from $(C_1-C_6)alkylthio$, $(C_1-C_6)alkoxy$, $trifluoromethyl$, $halo$, CN , $(C_6-C_{10})aryl$, $(C_2-C_9)heteroaryl$, $(C_6-C_{10})arylamino$, $(C_6-C_{10})arylthio$, $(C_6-C_{10})aryloxy$, $(C_2-C_9)heteroarylamino$, $(C_2-C_9)heteroarylthio$, $(C_2-C_9)heteroaryloxy$, $(C_6-C_{10})aryl$, $(C_6-C_{10})aryl$, $(C_2-C_6)cycloalkyl$, $hydroxy$, $piperazinyl$, $(C_6-C_{10})aryl$, $(C_1-C_6)alkoxy$, $(C_2-C_9)heteroaryl$, $(C_1-C_6)alkoxy$, $(C_1-C_6)acylamino$, $(C_1-C_6)acylthio$, $(C_1-C_6)acyloxy$, $(C_1-C_6)alkylsulfinyl$, $(C_6-C_{10})arylsulfinyl$, $(C_1-C_6)alkylsulfonyl$, $(C_6-C_{10})arylsulfonyl$, $amino$, $(C_1-C_6)alkylamino$ or $[(C_1-C_6)alkyl]_2amino$;~~
- ~~— R^7 is hydrogen; $(C_1-C_6)alkyl$ optionally substituted by one or more of hydroxy, CN , $(C_1-C_6)alkylamino$, $(C_1-C_6)alkylthio$, $(C_1-C_6)alkoxy$, $perfluoro(C_1-C_6)alkyl$, $(C_6-C_{10})aryl$, $(C_6-C_{10})arylthio$, $(C_6-C_{10})aryloxy$, $(C_2-C_9)heteroarylamino$, $(C_2-C_6)cycloalkyl$, $(C_1-C_6)alkyl(hydroxymethylene)$, $piperidyl$, $(C_1-C_6)alkylpiperidyl$, $(C_1-C_6)acyl$, $(C_1-C_6)acylamino$, $(C_1-C_6)acyloxy$, $(C_1-C_6)alkoxy(C=O)$, CO_2H , $(C_1-C_6)alkylNH(C=O)$, and $[(C_1-C_6)alkyl]_2N(C=O)$; $(C_6-C_{10})arylsulfonyl$, $(C_1-C_6)alkylsulfonyl$, $(C_1-C_6)alkylNH(C=O)$; $(C_1-C_6)alkoxy(C=O)$; $(C_1-C_6)alkyl(C=O)$; $[(C_1-C_6)alkyl]_2N(C=O)$; or $(R^8R^9N)(C=O)$ where R^8 and R^9 are taken together with the nitrogen that they are attached to form a ring selected~~

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from azetidiny!, pyrrolidiny!, piperidiny!, morpholinyl and thiomorphonyl;
where Q is (C₆-C₁₀)aryl(C₁-C₆)alkoxy(C₆-C₁₀)aryl, (C₆-C₁₀)aryl(C₁-
C₆)alkoxy(C₁-C₁₀)heteroaryl, (C₁-C₁₀)heteroaryl(C₁-C₆)alkoxy(C₆-
C₁₀)aryl, or (C₁-C₁₀)heteroaryl(C₁-C₆)alkoxy(C₁-C₁₀)heteroaryl;
~~with the proviso that when X is SO or SO₂ and R₃ and R₄ are a substituent~~
~~comprising a heteroatom, the heteroatom cannot be bonded to the ring;~~
~~and with the proviso that at least one of R¹-R⁶ must be (C₁-C₆)alkyl;~~
~~and with the proviso that when X is oxygen or sulfur and R³-R⁶ are each hydrogen~~
~~then R¹ and R³ cannot both be methyl;~~
that possesses an in vitro IC₅₀ selectivity for TACE over MMP-1 of at least 100
fold; wherein MMP-1 activity is determined by an MMP-1 in vitro assay
and wherein TACE activity is determined by a human monocyte assay.
Claims 62 – 83 (Cancelled)